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1 : *Br J Pharmacol* 1995 Oct;116(4):2298-302

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## **The effect of a synthetic 7-thiaprostaglandin E1 derivative, TEI-6122, on monocyte chemoattractant protein-1 induced chemotaxis in THP-1 cells.**

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1 The ability of various prostaglandins (PGs) to inhibit monocyte chemotaxis induced by monocyte chemoattractant protein-1 (MCP-1) was investigated with a human monocytic leukaemia cell line, THP-1. Moreover, to investigate the mechanism of the inhibitory action of PGs the involvement of either intracellular adenosine 3': 5'-cyclic monophosphate (cyclic AMP) accumulation or intracellular Ca<sup>2+</sup> mobilization was studied. 2 TEI-6122, a synthetic 7-thia-PGE1 derivative, inhibited chemotaxis of THP-1 cells induced by MCP-1 with an IC<sub>50</sub> of 1.5 pM. Its inhibitory activity was 1000 fold more than that of PGE1 and PGE2 (IC<sub>50</sub> = 2.8 nM and 0.9 nM, respectively), which were more potent than other PGs such as PGA1, PGA2, PGF2 alpha and PGI2 (IC<sub>50</sub> > or = 1 microM). 3 With respect to the effect on intracellular cyclic AMP accumulation in THP-1 cells, TEI-6122 was as potent as PGE1 and PGE2, which were approximately 100 to 1000 fold more potent than the other PGs such as PGA1, PGA2 and PGI2. The minimum concentration of TEI-6122 required to increase intracellular cyclic AMP accumulation in THP-1 cells was 1 nM. 4 TEI-6122 and PGE1 (4 microM) transiently increased intracellular calcium levels in THP-1 cells. When added prior to MCP-1, both PGs partially suppressed the increased in Ca<sup>2+</sup> caused by this cytokine. There were no significant differences between the activity of TEI-6122 and PGE1 in either respect.

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Revised: January 10, 2000.

Art Unit: 1644

of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

b. Claim 5 recites the term "capable of producing...". The specification is non-enabling for polynucleotides that do not produce TWIK1 and are only capable of, if further modified such that they can produce TWIK1, because Applicant has not taught how to further modify polynucleotides such that they can produce TWIK1. It has been held that an element is "capable of" performing a function is not a positive limitation but only requires the ability to perform. It does not constitute a limitation in any patentable sense. In re Hutchinson, 69 USPQ 138. Applicant is advised to substitute the term "encoding" for "capable of producing".

***Claim Rejections - 35 USC § 112 second paragraph***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

a. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2(i) recites the term "stringent hybridization conditions", which is a conditional term and renders the claim indefinite. Furthermore, some nucleic acids which might hybridize